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EXAMINER	
BORIN, MICHAEL L	

ART UNIT	PAPER NUMBER
1631	

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07/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,131	OFER, DROR	
	Examiner	Art Unit	
	Michael Borin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04/22/2009* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25,29-57,102,103,155-159 and 161-163* is/are pending in the application.

4a) Of the above claim(s) *7,10-13,16-23,37-39,50-53,57,102,103 and 157* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9,14,15,24,25,29-36,40-49,54-56,155,156,158,159 and 161-163* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-25,29-57,102,103,155-159,161-163 are pending. Claims 7,10-13,16-23,37-39,50-53,57,102,103,157 remain withdrawn from consideration. Claims 1-6,8,9,14,15,24,25,29-36,40-49, 54-56,155,156,158,159,161-163 are under examination.

2. Response filed 04/22/2009 is acknowledged. In response to Examiner's request, Applicant clarifies that the step of "performing a plurality of assays" is directed to *in vitro* analytical assays.

Applicant's arguments have been fully considered and were deemed to be persuasive-in-part. Rejections not reiterated from previous Office actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-6,8,9,14,15,24-36,40-49,54-56,155,156,158-163 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons and is necessitated by amendment.

A. Per applicant's clarification in the In the response of 04/22/2009, the assaying is *in vitro*, rather than *in silico.* Then, it is not clear how *in vitro* assays will measure interaction with geometrical triangular structures used to described the compounds used in the assays. For example, it is not clear how functional and binding assays addressed on p. 30-31 of specification, e.g., a replication assay for DNA target (see p. 31, top),katie can be used to characterize interaction with a triangular substructure used to describe a compound.

B. Further, since the active method step of the method is performing *in vitro* assays, i.e., interacting compounds with target molecule, it is not clear what relevance in such case have claim limitations addressing "triangular geometric structures", "triangular space", which are features addressing *in silico* modeling, rather than *in vitro* testing. As addressed by applicant in response of 12/03/2008, p. 15, "the "triangular geometric substructure" in amended claim 1 describes a feature of a model of a molecule, rather than a feature of a molecule"

C. Claim 1 now addresses performing a plurality of assays for measuring an interaction of target with gauges. First, as claim is amended to read on compounds comprising gauges, it is not clear whether the assaying is performed with compounds or with gauges. Second, inasmuch as the assays are *in vitro* assays, it is not clear how *in*

vitro assay, e.g., a functional assay, measures interaction with a geometrical feature of a compound.

Same applies to claims 29-31, 44-46.

D. Claim 5: The claim lacks antecedent basis, as claim 1 does not address a "target active area".

E. Claims 44-49: The claims are directed to binding of certain number of gauges and identifying certain amount of different configurations. In the absence of further defining of the area to be assayed, how one can know of amount of gauges that successfully bind to target, or amount of different configurations to be discovered by the method prior to applying the method itself.

It is noted that applicant, in response to rejections K, and L (pages 23-24 of the response of 12/03/2008) discusses densities of gauges in triangular space. However, as addressed above, the claims do not read anymore on *in silico* assaying in triangular space; rather the claims address *in vitro* assaying using chemical compounds, rather than model gauges.

Claim Rejections - 35 U.S.C. § 101

4. Rejection of claims 1-6,8,9,14,15,24-35,40-49,54-56,155,156,158-163 under 35 U.S.C. 101 as being directed to non-statutory subject matter is withdrawn in view of applicant's clarification that the assaying addressed in the claims is *in vitro* assaying.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-6,8,9,14,15,24-35,40-49,54-56,155,156,158-163 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The rejection is applied for the following reasons:

A. Claim 1 introduces new matter as it addresses

"compounds comprising a set of … gauges, each of said gauges comprising at least one set of three binding points"

While specification addresses chemical gauges and uses of libraries thereof in *in* silico methods, it does not address compounds as being comprised of a set of gauges

B. Claim 1 introduces new matter as it addresses:

"analyzing said assay results using a plurality of said triangular geometric substructures".

As the assays, as now clarified, are *in vitro* assays, specification does not disclose using triangular geometric substructures to analyze *in vitro* assay results.

C. Claim 1 introduces new matter as it addresses: "triangle space defining all possible 3-point pharmacophores,… wherein said 3-point pharmacophore represents a set of three binding points on a molecule to which a gauge may bind". The specification does not address a triangle space as defined by possible 3-point pharmacophores.

Same applies to claims 6-8.

Claim Rejections - 35 USC § 103

6. Claims 1-4,26,29,29-33,36,41-46,155,156,158,159,161 are rejected 35 U.S.C.103(a) as obvious over Fejzo et al. (The SHAPES strategy: an NMR-based approach for lead generation in drug discovery. Chemistry & Biology , Volume 6 , Issue 10 , Pages 755 – 769, 2000; see IDS) in view of Pickett et al. (J. Chem. Inf. Comput. Sci. 1996, 36, 1214-1223) and also in view of Mason et al. (Pacific Symposium on Biocomputing 5:573-584, 2000)

The claims are drawn to method of obtaining information about a chemically active area of a target molecule, comprising assaying interaction of the target molecule with plurality of "gauges" (pharmacophores), wherein the gauges can be described as comprising at least one set of three binding points in a substantially rigid triangular configuration, and having at least one triangular geometric substructure defined by a triplet of distances that form a triangle and by a triplet of chemical binding point types for the triangle vertices.

In the response of 04/22/2009, applicant clarified that the assaying is *in vitro*, rather than *in silico.*

Fejzo et al. teach method of obtaining information about a chemically active area of a target molecule, comprising

- providing a set of diverse library of small molecules. See Fig 1, for example. The molecules therein are all substantially rigid structures as they all have aromatic rings. The latter aromatic moieties all comprise what is addressed in the instant claims as "substantially rigid triangular geometric substructure, because any 6-member ring can be envisioned as comprising "triangular substructures of binding points" - e.g., triangular substructure connecting positions 1,3 and 5 of a 6-member ring. Further, the reference teaches that the compound scaffolds are derived from the shapes commonly found in known therapeutic agents (Abstract) and p. 756, right column.
- assaying said interaction of said gauges with said target . See p. 759-762.
- analyzing said assay results to obtain information about said chemically active area. See p. 759-763.

With regard to characterization of the space in which the assaying occurs as "triangular space" or "space being defined as spanned by triangular configurations" , it should be noted that applicant clearly delineated in the response of 04/22/2009 that "*the*

step of "performing a plurality of assays" is directed to in vitro analytical assays" . Therefore, although *in vitro* conditions, e.g., a solution, can be addressed using identifiers such as "triangular space" or "space being defined as spanned by triangular configurations", such identifiers do not provide patentable distinction of the same *in vitro* space. In other words, a solution will remain the same solution, even if it is addressed as "triangular space". To this end, these limitations are not given patentable weight in applying prior art.

Fejzo et al do not teach all the characteristics of the testing "gauges" as instantly claimed, i.e., that the gauges can be described as comprising at least one set of three binding points in a substantially rigid triangular configuration, and having at least one triangular geometric substructure defined by a triplet of distances that form a triangle and by a triplet of chemical binding point types for the triangle vertices.

However, it is known in the art that pharmacophores can be described in terms of their geometrical characteristics, e.g., their 3-point or 4-point descriptors. See, for example, Mason et al., Abstract, p. 573, and Gig. 1. In particular, Pickett et al. teach 3-point descriptors for pharmacophores pharmacophore methods using a 3D distance space with three point combinations of pharmacophoric groups. .Each pharmacophore is defined by a triangular substructure of three atom/substructure centers. See Abstract, pages 1217-1218. Thus, each pharmacophore is can be addressed as the instantly claimed "gauge" comprising at least one set of three binding points in a substantially rigid triangular configuration, and having at least one triangular geometric substructure

defined by a triplet of distances that form a triangle and by a triplet of chemical binding point types for the triangle vertices.

Applying the KSR standard of obviousness, Examiner concludes that the combination of Pickett and Fejzo is applying a known technique to a known method.

One of ordinary skill in the art would have been capable of applying particular known techniques of characterizing pharmacophores, that are recognized as part of the ordinary capabilities of one skilled in the art, to a known method that was ready for such improvement in characterization, and the results would have been predictable to one of ordinary skill in the art. Further, since 3-point triangular descriptors are known as descriptors used in addressing pharmacophores, it would be obvious that such descriptors can be utilized in describing ligand-target molecule interaction in the method of Fejzo.

Further, with respect to claim 26, the reference teaches juxtaposition of side chains and scaffolds. See p. 256, right column, first full paragraph.

Further, with respect to claims 41-43 , the reference describes proteins used. See p. 756, second full paragraph; p. 761, left column)

Further, with respect to claims 32,33, the reference teaches at least 41 scaffold with 30 most common side chains. see p. 756, right column, second full paragraph.

Further, with respect to claim 36, see p. 763, first paragraph, and Fig. 6.

Further, with respect to claims 155, 156,161, the reference teaches assaying such proteins as p38 MAP kinase, and inosine-5-monophosphate dehydrogenase. p. 756, second full paragraph

Response to arguments

Applicant argues, in part (a) of the argument that that the library of Fejzo does not satisfy the “gauges” criteria in triangular space as addressed in the claims. However, inasmuch as applicant clarified in the response of 04/22/2009 that the step of "performing a plurality of assays" is directed to in vitro analytical assays using identifiers such as “triangular space” or “space being defined as spanned by triangular configurations” in addressing *in vitro* environment, such as e.g., a solution, such identifiers do not provide patentable distinction of the same *in vitro* space. In other words, a solution will remain the same solution, even if it is addressed as “triangular space”. To this end, these limitations are not given patentable weight in applying prior art.

In part (b) of the argument, applicant asserts that Fejzo et al. neither teaches nor suggests using triangular geometric substructures in analysis. However, as reflected in

the rejection, since 3-point triangular descriptors are known as descriptors used in addressing pharmacophores, it would be obvious that such descriptors can be utilized in describing ligand-target molecule interaction in the method of Fejzo.

Conclusion.

7. No claims are allowed

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Borin, Ph.D./
Primary Examiner, Art Unit 1631

mlb